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Claim Rejections – 35 USC §112

In the Office Action of 17 December 2004, Claims 9-19 are rejected under 35 USC 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

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It was asserted that in claims 1 and 3, the preamble recitation of "chelate-fluorophore tracer composition" is indefinite because it appears that a fluorophore is not a required claim limitation. For example, if both R1 and R2 are H, then the composition does not contain a fluorophore. Applicant has amended claims 1 and 3 to require that R1 must be H when R2 is $p\text{-CH}_2\text{C}_6\text{H}_4\text{-X-Y}$ and conversely, R2 must be H when R1 is $p\text{-CH}_2\text{C}_6\text{H}_4\text{-X-Y}$. Antecedent basis for amendment is found throughout the specification, wherein applicant specifies chelates covalently linked to a fluorophore (as in paragraph 0008 of the published Application US 2002/0072625, for example). A description of representative fluorophores that, when incorporated in compositions of the present invention, constitute molecular subunits of chelate-fluorophore tracer compositions of the present invention is provided in paragraph 0035 of the published Application, and methods for the covalent attachment of a fluorophore and a chelating agent are disclosed in paragraph 0037 of the published Application, as well as in Figure 4 of the Application. Example 1 of the Application provides a disclosure of an embodiment of the present invention in which a chelate-fluorophore tracer composition was prepared by linking fluorescein (a fluorophore) to EDTA. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

It was asserted that the recitation of "fused into a ring system" is indefinite because it is not clear whether R3 and R4 are fused into the same ring system or are each fused into a separate ring system. Applicant has amended the claims incorporating this recitation to specify

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that in certain embodiments of the claimed invention, R3 and R4 are fused into a cyclohexyl ring system. The cyclohexyl ring system is a single ring system, and in this embodiment, antecedent basis for which is provided as structure (H) of Figure 3, R3 and R4 are adjacent methylene groups that define one side of the six-membered cyclohexyl ring incorporated in a chelate-fluorophore molecule of the present invention. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

In claims 9-11, the recitation of "identical dilutions" is indefinite because it is not clear how dilutions are identical or what other dilutions are identical. The claims have been amended to specify the stepwise manner in which a first and a second series of serial dilutions of an aqueous solution thought to contain a macromolecular biological binding agent (claim 9), serum drawn from a target chelate-immunized animal (claim 10), or a hybridoma supernatant or a purified preparation of a monoclonal antibody (claim 11), respectively, are prepared; the manner in which combinations of each dilution of the first series of serial dilutions are prepared and analyzed for fluorescence polarization; the manner in which combinations of each dilution of the second series of serial dilutions are prepared and analyzed for fluorescence polarization; the manner in which the measured value of the polarization of the diluted solution containing the non-target tracer composition of the second series is subtracted from the measured value of the polarization of the diluted solution containing the target tracer composition of the first series, wherein the latter diluted solution has the same extent of dilution as the former diluted solution; and the manner in which the process is repeated for non-target metals. Antecedent basis for the amendments is drawn from the specification, for example, from Examples of the specification. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

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In addition, it was asserted that the recitation of "less than that producing a baseline signal for the target tracer composition" is indefinite because it is not clear what comparisons or mathematical operations, if any, are described. Applicant has amended claims 9-11 to particularly point out and distinctly claim his invention. Antecedent basis for the amendments is drawn from the specification, for example, from Examples of the specification. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

10 In claims 12-13 and 16-17, it was asserted, the recitation of "corresponding" is indefinite because it is not clear how correspondence is determined or what entities correspond. The claims have been amended to specify the stepwise manner in which a first and a second series of serial dilutions of an aqueous solution thought to contain a macromolecular biological binding agent (claim 9), serum drawn from a target chelate-immunized animal (claim 10), or a
15 hybridoma supernatant or a purified preparation of a monoclonal antibody (claim 11), respectively, are prepared; the manner in which combinations of each dilution of the first series of serial dilutions are prepared and analyzed for fluorescence polarization; the manner in which combinations of each dilution of the second series of serial dilutions are prepared and analyzed for fluorescence polarization; the manner in which the measured value of the
20 polarization of the diluted solution containing the non-target tracer composition of the second series is subtracted from the measured value of the polarization of the diluted solution containing the target tracer composition of the first series, wherein the latter diluted solution has the same extent of dilution as the former diluted solution; and the manner in which the process is repeated for non-target metals. Antecedent basis for the amendments is drawn
25 from the specification, for example, from Examples of the specification. Applicant submits that

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the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

In addition, it was asserted that the recitations of "this [polarization] value", "those produced" and "standard solutions" lack antecedent basis. Applicant has amended claims 12-13 and 16-17 to disclose the stepwise manner in which a first resulting solution is obtained by combining an aliquot of an aqueous solution (claim 12 and 13) or an aqueous extract (claims 16 and 17) is combined with a solution of EDTA or DTPA; a second resulting solution is obtained by combining the first resulting solution with a target chelate-fluorophore tracer composition; a third resulting solution is obtained by adding to the second resulting solution a third assay reagent that binds specifically to the target chelate-fluorophore tracer composition (claims 12 only); the fluorescence polarization of the last-mentioned resulting solution in each claim is measured; and the manner in which comparison is drawn between the fluorescence polarization of the last-mentioned resulting solution and the fluorescence polarization of each of a series of standard solutions that are prepared in a manner that is now disclosed in the claim. Antecedent basis for amendment may be found in Examples 4 and 8 of the specification, for example. By way of example, in Example 8 (paragraph 0115 of the published Application), applicant discloses a method for the preparation of a series of EDTA-Pb standard solutions, the method comprising serial dilution of a stock solution having a specific lead concentration, in this example 1 mM, with distilled water to give a set of standard solutions with final lead concentrations of 0, 20, 100, 200, and 500 ppt. The disclosure also provides steps in which a lead chelate-fluorophore conjugate prepared according to the present invention was added to each tube containing a standard solution, together with rabbit antiserum, to provide a series of resulting solutions that produced measurable fluorescence polarization; then in subsequent steps, the value of the mean polarization of each solution in the series was calculated and plotted against the chelate concentration in the corresponding lead standard solution, thus providing a standard curve for the determination of the

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concentration of lead in a test sample solution having an unknown lead concentration. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

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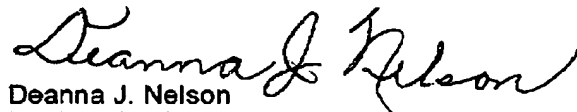
Allowable Subject Matter

Claims 9-19 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims. Applicant has rewritten claims 9-19 in independent form and has included all of the limitations of the base claim to which reference had been made and any
10 intervening claims that were rejected. Applicant submits that the claims, as amended, particularly point out and distinctly claim the subject matter which he regards as his invention, and respectfully requests examination of the amended claims.

Should additional information be required, Deanna J. Nelson is representing Applicant before
15 the Office. She is available by telephone at (919) 678-9478 during the hours of 8:00 AM to 4:00 PM Monday through Friday and by facsimile at (919) 678-9474.

Respectfully submitted,

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